FIGURE 1

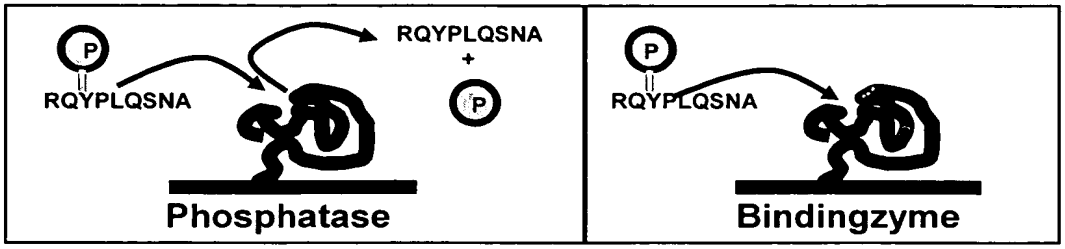


FIGURE 2

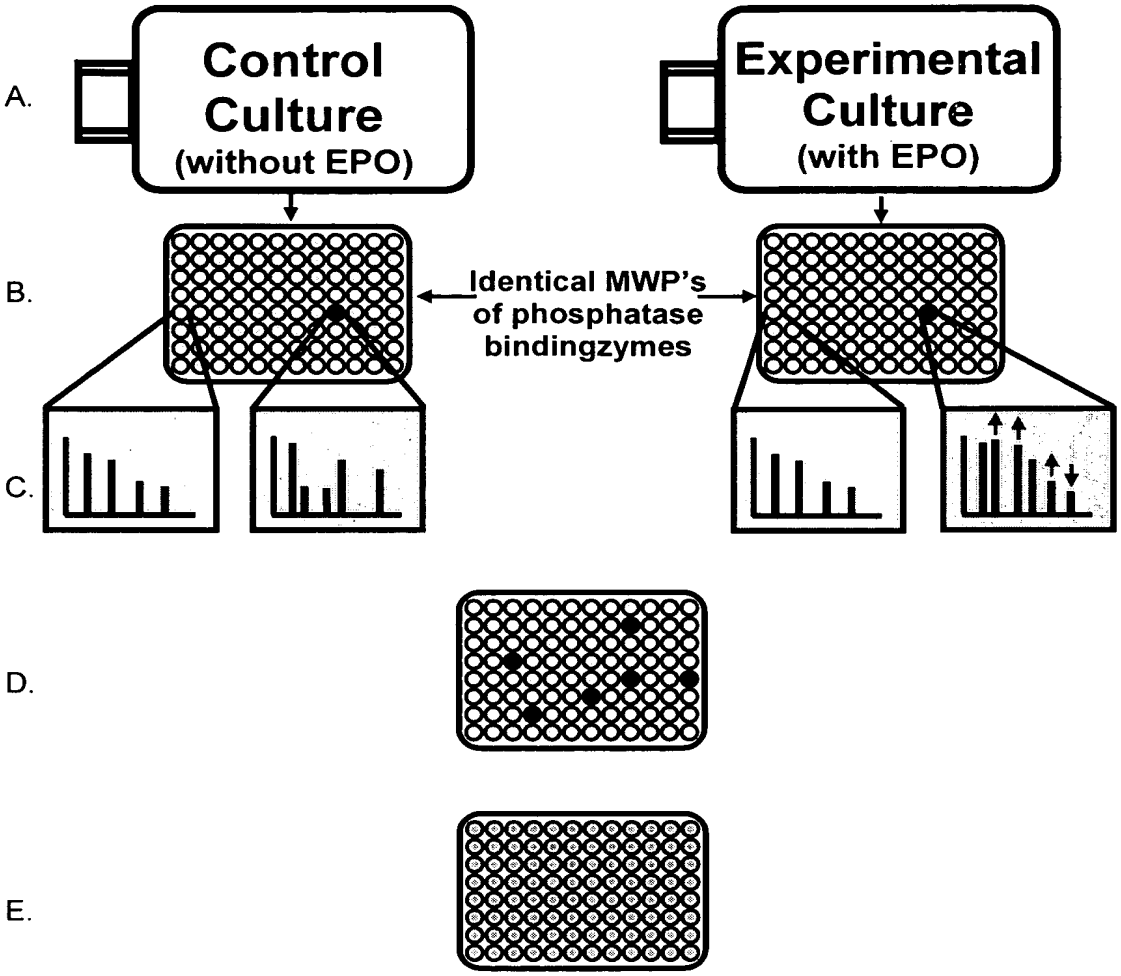

A.
Control Culture (without EPO)
Experimental Culture (with EPO)
B.
Identical MWP's of phosphatase bindingzymes
C.
D.
E.

FIGURE 3A

Bindingzyme	Gene ID	Variant	Peptide Length	Shortest	RefSeq ID	Aliases	Isoforms	Comment
1	PTPRC	1	1304	34	NM_002838	LCA, LY5, B220, CD45, T200, GP180	1	Regulates T- and B-cell signalling. Can activate Src family kinases and inhibit JAK kinases.
		2	1143		NM_080921		2	
		3	1256		NM_080922		3	
		4	34		NM_080923		4	
2	ACP1	1	70	70	NM_177554	HAAP, MGC3499	a	PTP and acid phosphatase
		2	158		NM_007099		b (Bs)	
		3	158		NM_004300		c, (Bf)	
3	PTP4A2	1	167	82	NM_003479	HH13, OV-1, PRL2, HH7-2, PRL-2, PTP4A, HU-PP-1, PTPCAAX2, ptp-IV1a, ptp-IV1b	1	Cancer Panel; C-terminal prenylation motif
		2	167		NM_080391		1	
		3	82		NM_080392		2	
4	PTP4A3	1	173	148	NM_032611	PRL3, PRL-3, PRL-R	1	Prenylated, All affect
		2	148		NM_007079		2	
5	PTP4A1		173	173	NM_003463	HH72, PRL1, PRL-1, PTPCAAX1, PTP(CAAX1)		Cancer Panel; Prenylated
6	PTPLA		288	288	NM_014241	PTPLA		adult & fetal heart
7	PTPN2	1	415	353	NM_002828	PTPT, TCPTP, TC-PTP, TCELLPTP	1	Substrates: EGFR & Shc
		2	387		NM_080422		2	
		3	353		NM_080423		3	
8	PTPN7	1	360	360	NM_002832	LPTP, HEPTP, PTPNI, BPTP-4, LC-PTP	1	TCR signalling; MAPK
		2	399		NM_080588		2	
		3	360		NM_080589		1	
9	PTPRO	1	1216	377	NM_030667	PTPU2, GLEPP1, PTP-U2	a	Variants exhibit tissue-specific expression. Isoforms c, d are candidates for the Cancer Panel.
		2	1188		NM_002848		b	
		3	405		NM_030669		c	
		4	377		NM_030668		d	
		5	405		NM_030671		c	
		6	377		NM_030670		d	

FIGURE 3B

Bindingzyme	Gene ID	Variant	Peptide Length	Shortest	RefSeq ID	Aliases	Isoforms	Comment
10	PTEN		403	403	NM_000314	BZS, MHAM, TEP1, MMAC1, PTEN1		Cancer Panel
11	PTPRR	1	657	412	NM_002849	PTPRQ, EC-PTP, PCPTP1, PTP-SL, PTPBR7	1	Neuronal growth and differentiation
		2	412		NM_130846		2	
12	PTPN1		435	435	NM_002827	PTP1B		Diabetes
13	PTPN11	1	593	460	NM_002834	CFC, NS1, SHP2, BPTP3, PTP2C, SHP-2, PTP-1D, SH-PTP2, SH-PTP3	1	In most tissues. Mutations associated w/Noonan syndrome.
		2	460		NM_080601		2	Under Review
14	PTPN18		460	460	NM_014369	BDP1		Cancer Panel
15	PTPN5		565	565	NM_032781	STEP, PTPSTEP, FLJ14427		Provisional RefSeq
16	PTPN9		593	593	NM_002833	MEG2		Phagocytosis
17	PTPN6	1	595	595	NM_002831	HCP, HCPH, SHP-1, HPTP1C, PTP-1C, SHP-1L, SH-PTP1	1	Hematopoietic cells
		2	597		NM_080548		2	
		3	624		NM_080549		3	
18	PTPRE	1	700	642	NM_006504	PTPE, HPTPE, R-PTP-EPSILON	1	RAS related pathways; SATA signaling; activation of voltage-gated K+ channels
		2	642		NM_130435		2	
19	PTPN22	1	807	691	NM_015967	LYP, Lyp1, Lyp2	1	Primarily Lymphoid tissues. Associates with CBL
		2	691		NM_012411		2	
20	PTPN12		780	780	NM_002835	PTPG1, PTP-PEST		Cancer Panel

FIGURE 3C

Bindingzyme	Gene ID	Variant	Peptide Length	Shortest	RefSeq ID	Aliases	Isoforms	Comment
21	PTPN3		913	913	NM_002829	PTPH1		Band 4.1 domain. P97 is a substrate. Regulated by adaptor protein 14-3-3 beta.
22	PTPN4		926	926	NM_002830	PTPMEG, PTPMEG1		Band 4.1 domain
23	PTPRN		979	979	NM_002846	IA2, IA-2, ICA512, R-PTP-N, IA-2/PTP		Diabetes
24	PTPRN2	1	1015	986	NM_002847	IAR, ICAAR, PTPRP, PHOGRIN, IA-2beta, KIAA0387, IAR PTPRP	1	Diabetes
		2	998		NM_130842		2	
		3	986		NM_130843		3	
25	PTPRH		1118	1118	NM_002842	SAP-1		Cancer Panel
26	PTPN21		1174	1174	NM_007039	PTPD1, PTPRL10		BMX/ETK interaction
27	PTPN14		1187	1187	NM_005401	PEZ, PTP36		Band 4.1 domain
28	PTPRJ		1337	1337	NM_002843	DEP1, SCC1, CD148, HPTPeta, R-PTP-ETA		(-) regulator of T-cell signalling
29	PTPRU	1	1436	1436	NM_133178	FMI, PTP, PCP-2, PTP-J, PTPRO, PTPU2, GLEPP1, PTP-PI, PTPPSI, hPTP-J, R-PTP-PSI, pi R-PTP-Psi	1	MAM domain. Neural development. Regulated by PMA in Jurkat cells.
		2	1440		NM_133177		2	
		3	1446		NM_005704		3	
30	PTPRK		1440	1440	NM_002844	R-PTP-kappa		MAM domain. Candidate for Cancer Panel
31	PTPRG		1445	1445	NM_002841	PTPG, HPTPG, RPTPG, R-PTP-GAMMA		Cancer Panel. CAH domain.

FIGURE 3D

Bindingzyme	Gene ID	Variant	Peptide Length	Shortest	RefSeq ID	Aliases	Isoforms	Comment
32	PTPRM		1452	1452	NM_002845	RPTPM, RPTPU, PTPRL1, hR-PTPu, R-PTP-MU		MAM domain
33	PTPRT	1	1463	1463	NM_133170	RPTPrho, KIAA0283	1	MAM domain. Central nervous system.
		2	1444		NM_007050		2	
34	PTPRD	1	1912	1501	NM_002839	HPTP, PTPD, HPTPD, HPTP-DELTA, R-PTP-DELTA	1	Neuron growth, axon guidance
		2	1899		NM_130391		2	
		3	1903		NM_130392		3	
		4	1501		NM_130393		4	
35	PTPRS	1	1948	1501	NM_002850	PTPSIGMA	1	Axonogenesis and nerve repair.
		2	1910		NM_130854		2	
		3	1501		NM_130853		3	
		4	1505		NM_130855		4	
36	PTPN23		1636	1636	NM_015466	HDPTP, HD-PTP, KIAA1471, DKFZP564F0923		Predicted RefSeq
37	PTPRF	1	1897	1888	NM_002840	LAR	1	Diabetes
		2	1888		NM_130440		2	
38	PTPRB		1997	1997	NM_002837	PTPB, HPTPB, HPTP-BETA, R-PTP-BETA		Implicated in cell adhesion, neurite growth, and neuronal differentiation.
39	PTPN13	1	2485	2294	NM_080683	PNP1, FAP-1, PTP1E, PTPL1, PTPLE, PTP-BL, PTP-BAS	1	Potential role in Fas-mediated programmed cell death; Rho signaling pathway
		2	2466		NM_006264		2	
		3	2294		NM_080684		3	
		4	2490		NM_080685		4	

FIGURE 4A
Candidate PTPS

Phosphatase	Genbank accession number	Coding sequence (bp)	Isolated from	MW wildtype (KDa)	MW fusion proteins GST / MBP	Mutant 1	Mutant 2	Double Mutant
He PTP variant 1	NM 002832	1,083 bp	Jurkat	40.5	66.5 / 82.5	D257A	Q335A	D257A Q335A
He PTP variant 2	NM 080588	1,200 bp	Jurkat	45.0	71.0 / 87.0	D296A	Q374A	D296A Q374A
MEG2	NM 002833	1,782 bp	Jurkat	68.0	94.0 / 110.0	D470A	Q559A	D470A Q559A
PTEN	NM 000314	1,212 bp	Jurkat	47.2	73.2 / 89.2	D92A	C124A	D92A C124A
SHP2 variant 1	NM 002834	1,782 bp	Jurkat	68.1	94.1 / 110.2	D425A	Q526A	D425A Q526A
SHP2 variant 2	NM 080601	1,383 bp	Jurkat	52.8	78.8 / 94.8	D425A	—	D425A —
TCPTP variant 1	NM 002828	1,248 bp	Jurkat	48.5	74.5 / 90.5	D182A	Q260A	D182A Q260A
PEST*	NM 002835	**1,041 bp**	K562	40.6	66.6 / 82.6	**D199A**	**Q278A**	D199A Q278A
PTP1B	M33689	**1,308 bp**	K562	50.0	76.0 / 92.0	**D181A**	**Q262A**	D181A Q262A

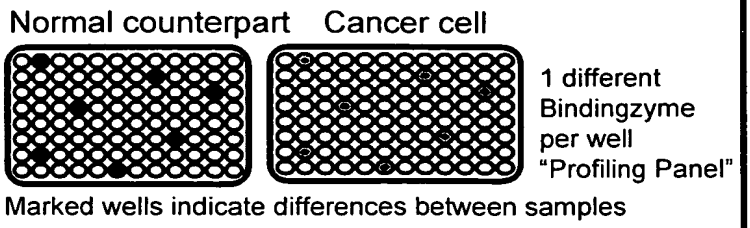
FIGURE 4B

PCR and Mutagenesis Primers

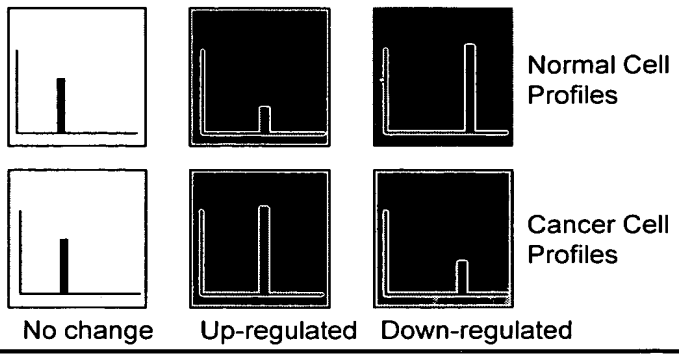
Phosphatase	PCR forward	PCR reverse	Mutant 1	Mutant 2
HePTP Variant 1	GAC GGA TCC ATG GTC CAA GCC CAT GGG	CAG GTC GAC TCA GGG GCT GGG TTC CTC	G GCC TGG CCA **GCC** CAT CAG ACA CCA	A GGG GGG ATG ATC **GCG** ACG GCA GAG CAG T
HePTP variant 2	GAC GGA TCC ATG GGA GCC TCC TTC TGG	CAG GTC GAC TCA GGG GCT GGG TTC CTC A	G GCC TGG CCA **GCC** CAT CAG ACA CCA	A GGG GGG ATG ATC **GCG** ACG GCA GAG CAG T
MEG2	ATA GAA TTC ATG GAG CCC GCG ACC GC	ATA TCT AGA TTA CTG ACT CTC CAC GGC CAG	TTG AGC TGG CCA **GCC** TAT GGT GTC CCT TC	G GCC TTC AGC ATC **GCG** ACC CCT GAG CAG T
PTEN	GAC GAA TTC ATG ACA GCC ATC ATC AAA GAG	CAG TCT AGA TCA GAC TTT TGT AAT TTG TGT ATG C	CA CAA TAT CCT TTT GAA **GCC** CAT AAC CCA CCA CAG	T CAT GTT GCA GCA ATT CAC **GCT** AAA GCT GGA AAG GGA CG
SHP2 variant 1	GAC GAA TTC ATG ACA TCG CGG AGA TGG	CAG TCT AGA TCA TCT GAA ACT TTT CTG CTG TTG	G ACC TGG CCG **GCC** CAC GGC GTG C	C CAG CAT TAT ATT GAA ACA CTA **GCG** CGC AGG ATT GAA GAA GAG
SHP2 variant 2	GAC GAA TTC ATG ACA TCG CGG AGA TGG	CAG TCT AGA TCA CCT GCA GTG CAC CAC	G ACC TGG CCG **GCC** CAC GGC GTG C	—
TCPTP variant 1	GAC GAA TTC ATG CCC ACC ACC ATC GAG	CA GGT CGA CAT TGT TTA TAG GGC ATT TTG CT G	T TAT ACT ACC TGG CCA **GCT** TTT GGA GTC CCT GAA T	AC CGA ATG GGT CTT ATT **GCG** ACC CCA GAT CAA CTG AG
PEST	GAC GGA TCC **ATG GAG CAA GTC GAG ATC CTG**	CAG GTC GAC TCA TTC AAC AAG GCA ACT GCG GG	TAT GTG AAC TGG CCVA **GCC** CAT GAT GTT CCT TCA TC	CA CAA AGG CAT TCT GCA GTA **GCA** ACA AAG GAG CAA TAT GAA CT
PTP1B	GAC GGA TCC **ATG GAG ATG GAA AAG GAG TTC G**	CAG GTC GAC CTA TGT GTT GCT GTT GAA CAG G	T ACC ACA TGG CCT **GCC** TTT GGA GTC CCT G	G ATG GGG CTG ATC **GCG** ACA GCC GAC CAG C

FIGURE 5

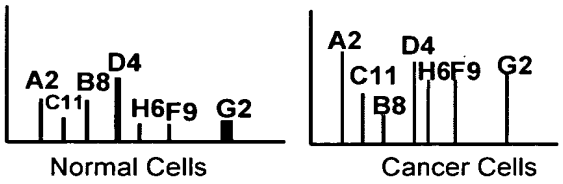
1. ***Profiling Panel*****: Different Bindingzyme each well; Duplicate Plates.** Lysates from cancer and normal cells are incubated with Profiling Panel to capture Phosphoproteins.



2. ***Identify Informative Bindingzymes*****:** Using MALDI-TOF MS, well-to-well comparisons of captured phosphoproteins are done to find those Bindingzymes that detect a difference between samples. (Spectra are simplified to convey concept.)



3. ***Screening Assay is Created:*** Informative Bindingzymes are combined to create the Screening Assay, which can detect all of the differences found by the Profiling Panel. Numbers above each peak refer to the original Profiling Panel position.



4. ***Screening Plate*****: Different lysate, same Informative Bindingzymes each well;** Lysates from cancer cells exposed to different compounds from a small molecule library are incubated with Screening Plates where each well contains the Screening Assay (identical set of Informative Bindingzymes).

5. ***Drug Candidates are Identified:*** Eluted phosphoproteins are analyzed by MALDI-TOF MS. Any compound that changes the cancer profile toward the normal cell profile is a drug candidate.